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10/563,110	06/19/2006	Hanne Muller	Q92287	1130

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EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
01/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/563,110	MULLER ET AL.	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-29, 33-43* is/are pending in the application.

4a) Of the above claim(s) *19,20,22,23,25,26,28,29,34,35 and 38-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,21,24,27,33 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants remarks filed on 13 October 2009 have been acknowledged and duly made of record.

Status of the Claims

Claims 18, 21, 24, 27, 33, and 36-38 are pending further prosecution on the merits. Claims 1-17 and 30-32 have been cancelled. Claims 19-20, 22-23, 25-26, 28-29, 34-35 and 38-43 have been withdrawn from further consideration.

Response to Arguments under 35 U.S.C. § 103(a)

Applicant's arguments filed on 13 October 2009 have been fully considered but they are not persuasive.

Applicants' amendment to the claims drawn to a phospholipid having c14 to c22 fatty acid side chains is no further distinguished than the limitation drawn simply to lipids in the last claim set of 19 February 2009.

Applicant attention is directed to page 5 in the last paragraph in the first three lines of the instant specification which cites that such lipids are generally c14 to c22 fatty acids.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.

1992). In this case, the teachings of Makula et al. sufficiently address the current limitation of claim 18 and all such claims depending therefrom.

Applicants argue that Lang does not directly teach EPA-containing PE. Applicants' arguments are considered but are not found persuasive because of the teachings of Yazawa et al. which clearly teach an EPA-containing PE such as PDE.

Applicants' argue that Sanigorski et al. is improper for allegedly failing to teach or suggest methanotrophic bacteria as sources of EPA-phospholipids and is silent to any potential medical use of saturated or monounsaturated fatty acid-containing compositions.

Applicants arguments are considered but are not found persuasive because Sanigorski et al. was not employed to suggest methanotrophic bacteria as sources of EPA-phospholipids or to expressly teach any potential medical use of saturated or monounsaturated fatty acid-containing compositions. Makula et al. was employed to overcome the limitation drawn to a methanotrophic bacterium which comprises PE and saturated and monounsaturated fatty acids from phospholipids. Koffas et al. was employed to indicate that the components of the invention are well-established as feeds for fish (please see page 8 at line 3 of the 1st paragraph).

For the reasons already made of record, the rejections of record are maintained in obviousness over the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 18, 21, 24, 27, 33, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang et al. Biomineralization of Magnetosomes in Bacteria: Nanoparticles with Potential Applications, printed pages 107-121 and Sanigorski et al. (Platelet and aorta arachidonic and eicosapentaenoic acid levels and in vitro eicosanoid production in rats fed high-fat diets, Lips. 1996 Jul; 31(7): 729-35. and Yazawa et al (Eicosapentaenoic acid-containing phospholipids for Feeds 1992, Jpn. Kokai Tokyo Koho, 5 pp. in view of Makula et al. (as already made of record) and Koffas et al. (2002/0137190 A1).

Lang et al. is employed to show evidence of the abundance of phosphatidylethanolamine identified in extracts of the magnetosome membrane from *M. gryphiswaldense,* which is a biomass (page 111, 2nd column, 2nd paragraph). The phrase, "*most abundant polar lipid[.]*" would reasonably constitute to the one of skill, a percentage of microbial lipid comparable to 80%wt (please see claim 36).

Lang et al. does not teach whereby plasma cholesterol levels are reduced.

However, Yazawa et al. teach [that] [t]he eicosapentaenoate-containing phospholipids such a as **phosphatidylethanolamine** and/or phosphatidylglycerol or microorganisms or algae producing them are used in feeds. Spontaneously hypertensive rats were fed a diet containing phosphatidylethanolmaine and phosphatidylglycerol (manufactured by fermentation of Alteromonas putrefaciens SCRC 2874) for 4 wk to show **lower** blood pressure, less fat accumulation, and **lower** hepatic and **plasma** triglyceride levels than those fed on **control** diet (abstract only).

Thus, Yazawa et al. establishes the nexus as to reasoning drawn to phosphatidylethanolamine and eicosapentaenoate (EPA), which is well-known in the art as an anticholesterolemic component.

Yazawa et al. does not teach the direct correlation directed to reducing cholesterol.

However, Sanigorski et al. teach the reasoning as to why it would be obvious to extract the lipids of Lang et al. which is further defined by Yazawa et al. as an eicosapentaenoate-containing phospholipid (EPA). EPA is art-known as a component in dual therapy with DHA in order to treat hypercholesterolemia. Sanigorski et al. teach the beneficial effects of the administration of EPA in animals administered this high-fat diet. Please see below:

> There is a significant interest in the interrelationship between long-chain n-3 and n-6 fatty acids due to their ability to modulate eicosanoid production. In general, the intake of arachidonic acid (AA) results in enhanced eicosanoid production, whereas n-3 polyunsaturated fatty acids (PUFA) decrease the production of eicosanoids from AA. **The purpose of this study was to investigate whether the effects of dietary AA on eicosanoid production in the rat were correlated with the AA and EPA levels in platelets and aorta (eicosanoid-producing tissues). Four groups of male Sprague-Dawley rats were fed a high-fat diet enriched with eicosapentaenoic acid (EPA)** and docosahexaenoic acid (DHA) (approximately 100 mg/day of EPA + DHA) for 24 d. During the last 10 d, the four groups were orally supplemented with 0, 30, 60, and 90 mg/day of ethyl arachidonate. A further group of rats was fed a control diet (without long-chain n-3 PUFA) for 24 d. In vitro aorta prostacyclin (PGI2) production, serum thromboxane A2 (TxA2) production and plasma, and platelet and aorta phospholipid (PL) fatty acids were measured. Enriching the diet with n-3 PUFA resulted in significant reductions in tissue AA levels and an increase in the n-3 PUFA, particularly EPA. On this diet, the AA to EPA ratio was 1:1 in platelet PL, and it was 2:1 in the aorta

> PL. There were significant decreases in the in vitro PGI2 and TxA2 production compared with the control animals. The inclusion of AA in the diet resulted in marked increases in AA levels in the platelet and aorta PL with corresponding decreases in EPA. The lowest dose of AA (30 mg/rat) reversed the effects of 100 mg/day of n-3 PUFA on AA levels in platelet and aortic PL and on in vitro aorta PGI2 and serum TxA2 production. The dietary AA caused a differential (twofold) increase in TxA2 relative to PGI2 for all three levels of AA supplementation. There were greater changes in the levels of AA and/or EPA in platelet PL compared with the aorta PL, which might have accounted for the differential effects of these PUFA on thromboxane production compared with PGI2 production in this study (printed pages 1 and 2, entire).

Accordingly, Makula teaches phospholipids of Methylococcus capsulatus, Methylosinus trichosporium, La Paz, and OBT were examined in relation to their qualitative and quantitative composition. M. Capsulatus exhibited a phospholipid composition consisting of **phosphatidylethanolamine**, phosphatidylglycerol, cardiolipin, and phosphatidyl-choline. The esterified fatty acids were predominantly C16:0 and C16: 1. M.trichosporium, La Paz, and OBT exhibited an essentially identical phospholipid composition consisting of phosphatidylmonomethylethanolamine, phosphatidyl-dimethylethanolamine, phosphatidylcholine, and phosphatidylglycerol. Only trace amounts (less than 1%) of cardiolipin were found in these organisms. The major esterified fatty acid in these organisms was C18: 1 (87 to 90%). The monounsaturated fatty acids from all four organisms consisted of both cis and trans isomers, each of which contained delta8, delta9, delta10, and delta11 double-bond positional isomers (Abstract only).

As disclosed above, Makula teaches phospholipids of Methylococcus capsulatus, Methylosinus trichosporium.

Makula et al. teach phosphatidylethanolamine, phosphatidylglycerol, cardiolipin, and phosphatidyl-choline.

Additionally, Makula et al. teach esterified fatty acids as being predominantly C16:0 and C16: 1.

Makula does not teach administration to fish or juvenile fish. Makula also does not teach a utility for phosphatidylethanolamine.

However, Koffas et al. (2002/0137190 A1) teach […] different livestock animal types may have different nutritional requirements in terms of the relative proportions of protein to carbohydrate. Many carnivorous aquatic **fish** species, for example, have very high protein requirements. Ruminant livestock, on the other hand, thrive on higher fiber/carbohydrate diets. Methylomonas 16a has the capacity to form large amounts of carbohydrate, under certain conditions, in addition to the cellular protein which is always produced. Genes involved in gluconeogenesis (glycogen formation) or glycogen degradation might be altered or regulated such that glycogen content could either be decreased or increased. Thus the composition of the crude cell mass could be modulated to target high protein markets (lower carbohydrate) or alternatively, higher carbohydrate lower protein feed markets. **The ability to engineer the composition of the microbe precludes the need to artificially formulate protein/carbohydrate ratios by exogenous additions** [0156].

Further Koffas et al. (0137190 A1) teach methods of administration [that] the present invention provides a unique methanotrophic bacterial strain, useful for the production of a variety of materials from C1 carbon sources such as methane and methanol. The strain is referred to herein as Methylomonas 16a, and is characterized by rapid doubling time, high yield and the presence of genes encoding both the Entner-Douderoff carbon pathway as well as the Embden-

Meyerhof pathway, allowing for versatility in carbon flux management and higher efficiency of carbon incorporation. The strain has been shown to produce a variety of food and feed products such as single cell protein, exopolysaccharide and starch. The strain has particularly high value in the production of food and feed materials as it is possible to manipulate the various concentrations of protein, carbohydrate and starch all within the same organism**. This capability will permit strains to be uniquely tailored for individual specific food and feed applications.** Additionally the strain has demonstrated utility in the production of terpenoid and carotenoid compounds, useful as pigments and as monomers in polymeric materials [0075].

Koffas et al. (0137190 A1) does not teach juvenile fish, however it is obvious based in the context of the teachings that any fish would have at one time been a juvenile fish being administered these same food and feed formulations.

Determining the scope and content of the prior art, instant claim 18 discloses nothing with regard to the extraction of a lipid component as cited in the current set of arguments. The method is directed to no specific target population/ classification of fish (as elected) or animal. Claim 18 is broad and not exclusive with regard to the target population treated. Thus, any reference teaching the feeding of PE to animals would be expected to achieve the same effects as taught in the invention. Phosphatidylethanolamine is abundant in a cell mass (biomass), which reasonably overcomes the limitation of claim 36.

In ascertaining the differences between the art and the claims at issue, the art teaches variable species of biomass and does not expressly equate the lipid extract of said biomass as being beneficial in reducing hypercholesterolemia. However, the references *supra* adequately

address the limitations drawn to a method of treatment to reduce plasma cholesterol levels based upon the reasoning of Yazawa et al. Further, the teachings of Makula et al. could reasonably be extended to microbial lipids based upon obviousness to try further modulation/extraction of lipid components in the normal course of due experimentation.

Objective evidence present in the application is drawn to a phospholipid which is abundant as an extract of crude cell mass. Yazawa et al. teach utility [that] [t]he eicosapentaenoate-containing phospholipids such a as **phosphatidylethanolamine** [...] are used in feeds. Lang et al. does not teach PE as being eicosapentaenoate-containing but based upon the plethora of nutrients to be extracted from a biomass as described in Lang et al. and in the general prior art, EPA could be reasonably interpreted as an element that may be magnetically aggregated. Sanigorski et al. establishes the beneficial effects of EPA-containing phospholipid such as PE as Yazawa establishes that the subject that may benefit may be marine life, (i.e., fish), but is also not exclusive to marine life.

Overall obviousness is reasonably recognized based upon what is clearly taught by the general biomass of Lang et al., which may be extended to include a plethora of variable nutrients as disclosed. Based upon Lang et al., Yazawa et al. provides further motivation by teaching PE which may be used in feeds. Sanigorski et al. provides reasoning as to why the teachings of Lang et al. could be extended to include the teachings of Yazawa. The procedure of extracting the biomass of Lang et al. would reasonably aggregate EPA containing phospholipids (as taught by Yazawa). This, in turn, would reasonably result in a perceived lowering in the cholesterol levels of said subjects having any form of ingestion of the particular component. Absent of any distinction or delineation clearly pointing out that this particular PE as claimed is essentially free

of any form of EPA (a known natural component to palliate hypercholesterolemia), instant obviousness should be reasonably apparent to the one of skill.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

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